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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/526,298	03/15/00	EVANS R	P41-9321

HM22/1020
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EXAMINER	
MCGARRY,S	
ART UNIT	**PAPER NUMBER**
1635	5

DATE MAILED: 10/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/526,298	Evans et al
Examiner	**Group Art Unit**
Sean McGarry	1635

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *14-19 and 35-53* is/are pending in the application.

Of the above, claim(s) *49-53* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *14-19 and 35-48* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *2*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 14-19 and 35-48, drawn to methods of modulating and inducing gene expression a subject, classified in class 514, subclass 44.

II. Claim 49, drawn to a method of distinguishing the physiological effect of a hormone receptor, classified in class 435, subclass 4.

III. Claims 50-52, drawn to a method of rendering a mammalian hormone receptor uniquely responsive to a ligand not endogenous to the mammal of the receptor, classified in class 435, subclass 4.

IV. Claim 53, drawn to a method to determine the ligands tom which orphan receptors respond, classified in class 435, subclass 6.

2. The inventions are distinct, each from the other because of the following reasons: Inventions I-IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are mutually exclusive methods that contain different methods steps where these methods steps use materially different compounds and where the method steps lead to different results.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

5. During a telephone conversation with Stephen Reiter on 10/04/00 a provisional election was made with traverse to prosecute the invention of Group I, claims 14-19 and 35-48. Affirmation of this election must be made by applicant in replying to this Office action. Claims 49-53 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

7. Claims 14-19 and 35-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a methods drawn to the induction or repression of a specific gene by a member of the steroid/thyroid superfamily of receptors which associates with at least the dimerization domain of ultraspiracle receptor, in the presence of ligand for said member, where the expression of said gene is maintained under the control of a hormone response element to which said member binds where the method comprises exposing the expression system to at least the dimerization domain of an ultraspiracle receptor where the method is in vitro or in cells in culture, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims drawn to nucleic acid based therapy.

Claims 14-19 and 35-48 are drawn to nucleic acid based therapies.

The instant claims are drawn to nucleic acid therapy and involve methods of introducing and expressing exogenous genes and nucleic acid sequences in specific cells in a whole animal. For example, the claims require the integration of a gene coding for an ultraspiracle receptor and/or the introduction of a construct containing the hormone response sequence where said construct would further comprise a desired exogenous gene to be regulated by the ultraspiracle receptor (see pages 10, 21, and 22 of the instant specification, for example).

The art of gene therapy is an unpredictable art that requires much guidance. The instant specification provide guidance for the instant methods in cells in culture but does not provide guidance or example that would show by correlation the instant methods as the are drawn to

nucleic acid based therapies. For example the instant specification fails to teach one of skill in the art how to integrate the gene construct for the exogenous ultraspiracle receptor to specific desired cells such that expression would be at a level adequate for inducing the expression of a gene under the appropriate hormone repone element. The targeting of specific cells would be required, for example in cases where as applicant contemplates and claims, a method of selectively killing cells and for directing expression of a desired gene in a specific cell type or tissue type. The instant specification fails to provide adequate guidance for one of skill in the art to create a "pre-existing system in an animal" and apply the instant methods. The establishment of such a system requires the introduction of an exogenous nucleic acid construct into cells of an animal and also to provide at least the dimerization domain of an ultraspiracle receptor where the exposure is disclosed in the specification to embrace exposing these cell at least the dimerization domain of an ultraspiracle receptor per se and also a DNA that encodes at least the dimerization domain of an ultraspiracle receptor.

The instant specification provides only skant and general guidance for introduction of genes to a whole animal and provide no specific guidance. Nucleic acid based therapy is an unpredictable art and one of skill in the art is in need of specific guidance for any specif gene therapy. The art has shown that there are no routine methods and has further shown that one cannot expect positive results using methods known today yet at the time of the instant invention. Ronald Crystal states [Science Vol. 270:404-410, 1995] at page 409 "[a]ll of the human transfer studies have been plagued by inconsistent results, the bases of which are unknown." Crystal

reviews the state of the art of gene therapy and discusses the obstacles that still remain to effect nucleic acid based therapies and discusses the potential of nucleic acid based therapies. Verma et al [Nature Vol. 389:239-242, 1997] discusses the problems of gene therapy artisan face even today. It is stated "[a]lthough more than 200 clinical trials are currently underway worldwide, with hundreds of patients enrolled, there is still no single outcome that we can point to as a success story." and further "[t]he choice of tissue in which to express the therapeutic protein will ultimately depend on considerations such as the efficiency of gene delivery, protein modifications, immunological status, accessibility and economics." and also"[t]he Achilles heel of gene therapy is gene delivery, and this is the aspect . . ." It is clear, that although gene therapy provides promise for the treatment of disease and applicants invention to would be promising in a gene therapy, there are general obstacles faced by the artisan in the practice of gene therapy where the instant specification fails to provide adequate guidance to overcome these obstacles to practice the instant invention. This position is further taken in view of the disclosure of Orkin et al where it is also discussed the many problems of gene therapy that need to be overcome (see numbered pages 1, 3-14 and 30-35). It is clear from the art that the art of gene therapy is unpredictable and the state of the art at the time of invention would require specific guidance for any particular gene therapy where no routine methods are known. One of skill in the art would need to overcome the basic problems addressed in the art to practice the instant invention as it relates to gene therapy.

8. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 recites "exogenous genes" on line 2. There is no antecedent basis for the plural "genes" in the context of the claim.

Claim 17 also recites "wild type genes" and therapeutic genes". The meaning of these terms is not clear. At page 17 of the specification it is asserted that a human insulin gene is considered to be a wild type gene in a skin fibroblast cell because even though it is not expressed at a biologically significant level they do contain the genetic material encoding human insulin. Therapeutic genes are defined as those that are not normally found in a host cell. It is then stated that a human insulin gene would be considered a therapeutic gene in human skin fibroblast cells. With the definition and examples given, one in the art would be incapable of determining what are therapeutic genes and what are wild type genes in the context of the instant claim.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean McGarry whose telephone number is (703) 305-7028.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached on (703) 308-4003.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. Papers should be faxed to Art Unit 1635 via the PTO Technology Center Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see C.F.R. 1.6(d)). The Art Unit 1635 FAX number is (703) 308-4242 or (703) 305-3014. NOTE: If Applicant **does** submit a paper by Fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

October 10, 2000

SEAN MCGARRY
PATENT EXAMINER
Technology Center 1600